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EXAMINER	
VATHYAM, SUREKHA	

ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,181	BARRINGER, GEORGE E.	
	Examiner	Art Unit	
	Surekha Vathyam	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/03, 11/04 & 01/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Drawings

1. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(4) because reference character "100" has been used to designate both a macromolecule preparation process (page 1, lines 11 – 12) and apparatus (page 6, line 15) and reference character "752" has been used to designate both waste site (page 13, line 1) and aseptic fluid interface apparatus (page 13, line 6).

2. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: "910" and "914".

3. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

4. The disclosure is objected to because of the following informalities:

5. Page 3, lines 28 – 30 and page 4 lines 1 – 2 should be corrected to read "Application of electric field 1008 causes differential motion of the charged molecules according to their electrophoretic mobilities, with cations 1002 and 1004 moving towards the cathode 1010. In the ideal case, the anions 1006 move to the anode 1012, though experimentally a phenomenon known as electroosmotic flow can reduce or reverse the anion to anode motion." The corrections to be made are the underlined terms; the specification has the anode and cathode reversed from the dictionary definition of the negatively charged electrode being the cathode and the positively charged electrode being the anode. According to the Webster's dictionary, the polarity as defined in the specification only applies in the case of batteries i.e., galvanic cells which is not the case in the current application.

6. Page 9, line 24 should read filter "416" and not "418".

7. The amendments to the specification received 06/21/2004 have the following errors: Page 5 of the amendments, paragraph beginning with "Fig. 7C depicts ...", line 12 should be corrected to read "preferably between filter 766 and valve 758" and not "preferably between flow sensor 718 and valve 758". Page 6 of the amendments, first full paragraph should refer to "page 15, line 28 through page 16, line 9" and not "page 16, line 28 through page 17, line 9". Page 7 of the amendments, second full paragraph should be corrected to refer to outlet valve 702 and not 703; outlet gate valve 702 and not 703; inlet gate valve 703 and not 702.

Appropriate correction is required.

8. Claim 23 is objected to because of the following informalities: lines 7 – 8 of claim 23 recite the phrase "from the macromolecule" twice. Appropriate correction is required.

9. Claim 41 is objected to because of the following informalities: line 11 of claim 41 has the word "lever" which should be corrected to "level". Appropriate correction is required.

10. Claim 45 is objected to because of the following informalities: line 8 of claim 45 has the phrase "filter s selected"; the letter "s" between filter and selected should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 3 and 5 recite the limitation "the sample source" in line 1 of each respective claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Note: While it is unclear what is being claimed, as discussed above, the claims have been considered with regard to the prior art to the extent possible.

14. Claims 1 – 9, 12 – 17, 19 – 20, 24 – 30, 33 – 34, 36 – 37, 39 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Swerdlow et al. (US 5,935,522).

Regarding claim 1, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: an inlet chamber (112); a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), one end of the column being fixed at the interior of the inlet chamber (column 8, lines 29 – 33); and a liquid source (102) adapted for automatic control (column 11, lines 53 – 62), that supplies a liquid sample through an input valve (108) into the inlet chamber (112), the sample supplied to be in fluid communication with the end of the column (column 10, lines 1 – 5).

Regarding claim 2, Swerdlow ('522) discloses the apparatus comprising an outlet valve (147) located at the inlet chamber (112).

Regarding claim 3, liquid flow between the inlet and outlet chambers occurs due to the inherent pressure differential between the two chambers. Nonetheless, Swerdlow ('522) discloses the apparatus wherein the sample source pressurizes the inlet chamber to create a pressure differential across the length of the column (column 10, lines 1 – 42).

Regarding claim 4, Swerdlow ('522) discloses the apparatus comprising an outlet chamber (120), the other end of the column being fixed at the interior of the outlet chamber (column 8, lines 39 – 42).

Regarding claim 5, Swerdlow ('522) further discloses the apparatus wherein the sample source pressurizes one chamber compared to the other chamber to create a

pressure differential across the length of the column (column 11, line 67 – column 12, line 5).

Regarding claim 6, Swerdlow ('522) further discloses the apparatus the liquid source further comprising a reservoir supplying a cleaning solution (column 12, lines 18 – 25).

Regarding claim 7, Swerdlow ('522) further discloses the apparatus the liquid source further comprising a mechanical pump (100).

Regarding claim 8, Swerdlow ('522) further discloses the apparatus comprising an output valve (147 and 122) at each chamber (112 and 120, respectively) that is controlled (130) to independently remove liquid from each chamber.

Regarding claim 9, Swerdlow ('522) further discloses the apparatus comprising at least one reservoir supplying a buffer (110), the liquid source independently supplying the buffer to the chambers (column 9, lines 61 – 67).

Regarding claim 12, Swerdlow ('522) further discloses the apparatus comprising electrophoresis electrodes coupled to an automatically controlled power supply (128) (column 5, lines 46 – 66 and column 11, lines 53 – 60).

Regarding claim 13, Swerdlow ('522) further discloses the apparatus comprising a heat exchanger in thermal contact with the column (column 11, lines 24 – 31).

Regarding claim 14, Swerdlow ('522) further discloses the apparatus comprising a degas unit that removes at least a portion of gas dissolved in the liquid (column 10, lines 16 – 20 and column 13, lines 22 – 35).

Regarding claim 15, Swerdlow ('522) further discloses the apparatus comprising an automated detector (118) that detects a molecular analyte in the liquid (column 11, lines 32 – 52).

Regarding claim 16, Swerdlow ('522) further discloses the apparatus wherein the detector is located at the column (column 8, lines 36 – 39).

Regarding claim 17, Swerdlow ('522) further discloses the apparatus comprising an automated controller (column 11, lines 53 – 60).

Regarding claim 19, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: a hydraulic system adapted for control by an automated controller (130), comprising a pump (100) and one or more valves (105, 108); a filter (106) selected to separate, at least in part, a macromolecule in a liquid mixture from one or more salt components in the mixture (column 9, lines 2 – 6); an inlet chamber (112) that receives a liquid sample, the sample comprising the macromolecule separated from the salt components (column 9, lines 46 – 49); a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), one end of the column being fixed at the interior of the inlet chamber (column 8, lines 29 – 33); and an automated controller (130) that controls the hydraulic system (column 11, lines 53 – 62) to create the liquid sample (column 7, lines 52 – 63), the sample comprising the macromolecule, by applying the liquid mixture to the filter (column 7, lines 63 – 67), with a pressure differential across the filter (column 7, lines 6 – 12), and to supply the sample to the inlet chamber (column 9, lines 46 – 49).

Regarding claim 20, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: a hydraulic system adapted for control by an automated controller (130), comprising a pump (100) and one or more valves (105, 108); a lysis unit (104) that is inherently capable of lysing cells in a liquid mixture comprising cells and a macromolecule; a filter selected to separate from the macromolecule, at least a portion of components in the mixture that are larger than the macromolecule (column 5, lines 36 – 40), the components comprising insoluble lysed cell components; an inlet chamber (112) that receives a liquid sample, the sample comprising a macromolecule separated from the insoluble lysed cell components; a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), one end of the column being fixed at the interior of the inlet chamber (column 8, lines 29 – 33); and an automated controller (130) that controls the hydraulic system (column 11, lines 53 – 62) to create the liquid sample (column 7, lines 52 – 63), the sample comprising the macromolecule, by applying the liquid mixture to the filter, with a pressure differential across the filter, and to supply the sample to the inlet chamber (column 9, lines 46 – 49).

Regarding claim 24, Swerdlow ('522) discloses a method for capillary electrophoresis (column 5, lines 47 – 66), comprising automatically supplying a liquid sample (column 6, lines 51 – 57) through a valve (108) to an inlet chamber (112) to place the sample in fluid communication with a capillary electrophoresis column (column

10, lines 1 – 5), the chamber having one end of the column fixed at the interior of the chamber (column 8, lines 29 – 33), and the column having a length of at least about 20 centimeters (column 10, lines 43 – 48).

Regarding claim 25, Swerdlow ('522) further discloses the method comprising pressurizing the inlet chamber (112) to create a pressure differential across the length of the column (column 10, lines 1 – 42).

Regarding claim 26, Swerdlow ('522) further discloses the method, the other end of the column being fixed at the interior of an outlet chamber (column 8, lines 39 – 43), further comprising directing fluid through the column by creating a pressure differential between the chambers (column 11, line 67 – column 12, line 5).

Regarding claim 27, Swerdlow ('522) further discloses the method comprising creating a pressure differential by electro-kinetic pumping (column 10, lines 29 – 42).

Regarding claim 28, Swerdlow ('522) further discloses the method comprising creating a pressure differential by mechanical pumping (column 10, lines 35 – 39 and column 15, lines 62 – 67).

Regarding claim 29, Swerdlow ('522) further discloses the method comprising independently directing liquid from each chamber to a waste site (column 10, lines 2 – 5 and column 12, lines 9 – 17).

Regarding claim 30, Swerdlow ('522) further discloses the method comprising independently supplying a buffer to each chamber (column 9, lines 61 – 67 and column 12, lines 9 – 17).

Regarding claim 33, Swerdlow ('522) further discloses the method comprising applying a voltage differential across the column to create electrophoretic flow in the column (column 10, lines 7 – 14).

Regarding claim 34, Swerdlow ('522) further discloses the method comprising cooling the column (column 11, lines 24 – 31).

Regarding claim 36, Swerdlow ('522) further discloses the method comprising detecting a molecular analyte in the liquid sample (column 11, lines 32 – 52).

Regarding claim 37, Swerdlow ('522) further discloses the method, the molecular analyte being a macromolecule (column 11, lines 32 – 36).

Regarding claim 39, Swerdlow ('522) discloses a method for capillary electrophoresis (column 5, lines 47 – 66), comprising automatically: acquiring a liquid mixture (column 6, lines 54 – 57), the mixture comprising a macromolecule (column 4, lines 18 – 23) and one or more salt components (column 8, lines 55 – 65); creating a liquid sample, the sample comprising the macromolecule (column 8, lines 25 – 27), by separating the macromolecule from at least a portion of the salt components (column 9, lines 39 – 45), by applying the mixture to a filter (106) with a pressure differential across the filter (column 7, lines 6 – 8) and supplying the liquid sample through a valve (108) to an inlet chamber (112) to place the sample in fluid communication with a capillary electrophoresis column (116) (column 9, lines 46 – 49), the chamber having one end of the column fixed at the interior of the chamber (column 8, lines 29 – 33), and the column having a length of at least about 20 centimeters (column 10, lines 43 – 48).

Regarding claim 44, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: means for automatically supplying a liquid sample (column 6, lines 51 – 57) through a valve (108) to an inlet chamber (112) to place the sample in fluid communication with a capillary electrophoresis column (116) (column 9, lines 46 – 49), the chamber (112) having one end of the column fixed at the interior of the chamber (column 8, lines 29 – 33), and the column having a length of at least about 20 centimeters (column 10, lines 43 – 48); and means for causing electrophoresis in the column (column 5, lines 46 – 66).

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. Claims 10 – 11, 21 – 22, 31 – 32, 35 and 41 – 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swerdlow et al. (US 5,935,522) in view of Goodale et al. (US 5,356,525).

Swerdlow ('522) discloses the apparatus as discussed with regards to claims 9 and 13 above.

Regarding claim 10, Swerdlow ('522) does not explicitly disclose a fluid level sensor at each chamber.

Goodale ('525) teaches a fluid level sensor (column 16, lines 25 – 43).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) to include a fluid level sensor in each chamber as taught by Goodale ('525) because Goodale ('525) explains it provides the benefit of detecting and controlling the level of liquid in the chambers (column 3, lines 56 – 60).

Regarding claim 11, Swerdlow ('522) further discloses the apparatus comprising a filter (106) to separate at least a portion of insoluble components from the liquid sample (column 9, lines 2 – 6), the liquid source applying the liquid to the filter with a pressure differential across the filter (column 9, lines 46 – 49).

Regarding claim 21, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: an inlet chamber (112) and an outlet chamber (120), the chambers each comprising an inlet valve (108, 122), an output valve (147, 122), and an electrode (column 16, line 64 – column 17, line 5), the electrodes

coupled to a power supply (128); a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), the opposite ends of the column being fixed at the interior of the respective chambers (column 8, lines 29 – 33 and column 8, lines 39 – 43); a liquid source comprising a pump (145,124) and at least one valved reservoir (114, 120) supplying a buffer, the liquid source being coupled to the input valves (147, 122); and an automated controller (130) that controls: the liquid source and at least one valve (122) to create a pressure differential (column 8, lines 39 – 43) across the length of the column (116) by pressurizing or depressurizing at least one chamber (120); the liquid source, the output valves (147, 122), the valved reservoir (114, 120), and the level sensors to independently: drain the chambers (column 10, lines 2 – 5); supply the chambers with liquid to place the liquid in fluid communication with the end of the column in each chamber (column 15, lines 53 – 67), including supplying: the buffer to the outlet chamber (column 12, lines 9 – 17); and independently to the inlet chamber (column 9, lines 61 – 67); the buffer and a liquid sample, the liquid sample comprising a macromolecule (column 9, lines 39 – 40); and a power supply (128) to apply a voltage differential across the column to cause electrophoresis of the macromolecule in the column (column 10, lines 7 – 11).

Swerdlow ('522) does not explicitly disclose a fluid level sensor at each chamber.

Goodale ('525) teaches a fluid level sensor (column 16, lines 25 – 43).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) to include a fluid level sensor in each chamber as taught

by Goodale ('525) because Goodale ('525) explains it provides the benefit of detecting and controlling the level of liquid in the chambers (column 3, lines 56 – 60).

Regarding claim 22, Swerdlow ('522) further discloses the apparatus comprising an automated detector (118).

Swerdlow ('522) discloses the method as discussed with regards to claims 30 and 34 above.

Regarding claim 31, Swerdlow ('522) does not explicitly disclose sensing the fluid level in at least one chamber.

Goodale ('525) teaches a method of fluid level sensing (column 16, lines 25 – 43).

It would have been obvious to one of ordinary skill in the art to have modified the method of Swerdlow ('522) to include fluid level sensing in at least one chamber as taught by Goodale ('525) because Goodale ('525) explains it provides the benefit of detecting and controlling the level of liquid in the chambers (column 3, lines 56 – 60).

Regarding claim 32, Swerdlow ('522) further discloses the method comprising separating at least a portion of insoluble components from the liquid sample (column 9, lines 2 – 6) by applying the liquid to a filter with a pressure differential across the filter (column 9, lines 46 – 49).

Regarding claim 35, Swerdlow ('522) does not explicitly disclose degassing at least a portion of gas dissolved in the liquid sample and the buffer.

Goodale ('525) teaches a method of degassing a liquid sample and buffer (column 8, line 57 – column 9, line 11).

It would have been obvious to one of ordinary skill in the art to have modified the method of Swerdlow ('522) to include degassing the liquid sample and buffer as taught by Goodale ('525) because it avoids the problem of "spikes" common in the art caused by bubbles in the sample as explained by Swerdlow ('522) (column 13, lines 22 – 35).

Regarding claim 41, Swerdlow ('522) discloses a method for capillary electrophoresis (column 5, lines 47 – 66), comprising automatically: supplying a liquid sample (column 6, lines 54 – 57) through a valve (108) to an inlet chamber (112) to place the sample in fluid communication with a capillary electrophoresis column (116) (column 9, lines 46 – 49): the chamber having one end of the column fixed at the interior of the chamber (column 8, lines 29 – 33); the column having a length of at least about 20 centimeters (column 10, lines 43 – 48); and the sample comprising a macromolecule (column 6, lines 57 – 62); directing fluid through the column by creating a pressure differential between the inlet chamber and an outlet chamber (column 11, line 67 – column 12, line 5), the other end of the column being fixed at the interior of the outlet chamber (column 8, lines 39 – 43); supplying a buffer to each chamber (column 9, lines 61 – 66 and column 12, lines 12 – 15); and directing liquid from each chamber to a waste site (column 10, lines 2 – 5 and column 12, lines 9 – 17); and electrophoretically

separating the macromolecule in the column by applying a voltage differential across the column (column 5, lines 46 – 66).

Swerdlow ('522) does not explicitly disclose sensing the fluid level in each chamber.

Goodale ('525) teaches a method of fluid level sensing (column 16, lines 25 – 43).

It would have been obvious to one of ordinary skill in the art to have modified the method of Swerdlow ('522) to include fluid level sensing in each chamber as taught by Goodale ('525) because Goodale ('525) explains it provides the benefit of detecting and controlling the level of liquid in the chambers (column 3, lines 56 – 60).

Regarding claim 42, Swerdlow ('522) further discloses the method further comprising detecting the macromolecule (column 11, lines 32 – 52).

18. Claims 18, 20, 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swerdlow et al. (US 5,935,522) in view of Petersen et al. (US 6,391,541).

Regarding claim 18, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: a hydraulic system adapted for control by an automated controller (130), comprising a pump (100) and one or more valves (105, 108); a rough filter selected to separate from a macromolecule in a liquid mixture, at least a portion of one or more rough components in the mixture that are larger than

the macromolecule (column 5, lines 36 – 41); a fine filter (106) selected to separate from the macromolecule, at least a portion of one or more fine components in the mixture that are smaller than the macromolecule (column 9, lines 2 – 6); an inlet chamber (112) that receives a liquid sample filtered by the rough and fine filters (column 9, lines 46 – 49), the sample comprising the macromolecule (column 9, lines 39 – 40); a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), one end of the column being fixed at the interior of the inlet chamber (column 8, lines 29 – 33); and the hydraulic system being controlled to create the liquid sample (column 11, lines 53 – 62), the sample comprising the macromolecule (column 4, lines 18 – 23), by applying the liquid mixture to each filter (column 4, lines 51 – 54), with a pressure differential across each filter (column 7, lines 6 – 8), and to supply the liquid sample to the inlet chamber (column 8, lines 26 – 29).

Swerdlow ('522) discloses the use of either a rough filter or a fine filter however Swerdlow ('522) does not explicitly disclose the use of both rough and fine filters in the apparatus.

Petersen ('541) teaches the use of both rough and fine filters (column 9, lines 14 – 20).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) to include both rough and fine filters as taught by Petersen ('541) because Petersen ('541) explains the rough filter has the benefit of filtering out coarse material while the fine filter filters out molecules smaller than the target macromolecule (column 9, lines 14 – 20).

Regarding claim 20, Swerdlow ('522) discloses an apparatus for capillary electrophoresis (abstract and Fig. 1), comprising: a hydraulic system adapted for control by an automated controller (130), comprising a pump (100) and one or more valves (105, 108); a filter selected to separate from the macromolecule, at least a portion of components in the mixture that are larger than the macromolecule (column 5, lines 36 – 40), the components comprising insoluble lysed cell components (column 9, lines 38 – 43); an inlet chamber (112) that receives a liquid sample, the sample comprising a macromolecule separated from the insoluble lysed cell components (column 9, lines 43 – 45); a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), one end of the column being fixed at the interior of the inlet chamber (column 8, lines 29 – 33); and an automated controller (130) that controls the hydraulic system to create the liquid sample (column 11, lines 53 – 62), the sample comprising the macromolecule (column 4, lines 18 – 23), by applying the liquid mixture to the filter (column 4, lines 51 – 54), with a pressure differential across the filter (column 7, lines 6 – 8), and to supply the sample to the inlet chamber (column 8, lines 26 – 29).

Swerdlow ('522) discloses a lysis unit (104) that is inherently capable of lysing cells in a liquid mixture comprising cells and a macromolecule; however, Swerdlow ('522) does not explicitly disclose the use of unit 104 as a lysis unit.

Petersen ('541) teaches a lysis unit (86).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) to include the lysis unit taught by Petersen ('541) because Petersen ('541) explains it helps rupture the cells and release the analyte therefrom for further analysis or purification (column 2, lines 1 – 3).

Regarding claim 38, Swerdlow ('522) discloses a method for capillary electrophoresis (column 5, lines 47 – 66) comprising automatically: acquiring a liquid mixture (column 6, lines 54 – 57), the mixture comprising a macromolecule (column 4, lines 18 – 23), one or more rough components that are larger than the macromolecule, (column 5, lines 36 – 41) and one or more fine components that are smaller than the macromolecule (column 8, line 55 – 66); creating a liquid sample, the sample comprising the macromolecule (column 8, lines 25 – 27), by separating from the macromolecule at least a portion of the components by applying the mixture to each of a plurality of filters (column 8, lines 25 – 27), with a pressure differential across each filter (column 7, lines 6 – 8), the filters comprising a rough filter selected to separate at least a portion of the rough components (column 5, lines 36 – 41) and a fine filter (106) selected to separate at least a portion of the fine components (column 9, lines 2 – 6); and supplying the liquid sample through a valve (108) to an inlet chamber (112) to place the sample in fluid communication with a capillary electrophoresis column (116) (column 9, lines 46 – 49), the chamber having one end of the column fixed at the interior of the chamber (column 8, lines 29 – 33), and the column having a length of at least about 20 centimeters (column 10, lines 43 – 48).

Swerdlow ('522) discloses the method of using either a rough filter or a fine filter however Swerdlow ('522) does not explicitly disclose using both rough and fine filters in the method.

Petersen ('541) teaches using both rough and fine filters (column 9, lines 14 – 20).

It would have been obvious to one of ordinary skill in the art to have modified the method of Swerdlow ('522) to include using both rough and fine filters as taught by Petersen ('541) because Petersen ('541) explains the rough filter has the benefit of filtering out coarse material while the fine filter filters out molecules smaller than the target macromolecule (column 9, lines 14 – 20).

Regarding claim 40, Swerdlow ('522) discloses a method for capillary electrophoresis (column 5, lines 47 – 66) comprising automatically: acquiring a liquid mixture (column 6, lines 54 – 57), the mixture comprising a macromolecule and one or more cells (column 17, lines 55 – 65); and creating a liquid sample, the sample comprising the macromolecule (column 8, lines 25 – 27), by separating from the macromolecule at least a portion of components larger than the macromolecule (column 5, lines 36 – 41), the components comprising insoluble lysed cell components, by applying the mixture to a filter (column 5, lines 36 – 41) with a pressure differential across the filter; and supplying the liquid sample through a valve (108) to an inlet chamber (112) to place the sample in fluid communication with a capillary electrophoresis column (116) (column 9, lines 46 – 49), the chamber having one end of

the column fixed at the interior of the chamber (column 8, lines 29 – 33), and the column having a length of at least about 20 centimeters (column 10, lines 43 – 48).

Swerdlow ('522) does not explicitly disclose lysing at least a portion of the cells.

Petersen ('541) teaches lysing cells (column 2, lines 1 – 3).

It would have been obvious to one of ordinary skill in the art to have modified the method of Swerdlow ('522) to include the step of lysing cells as taught by Petersen ('541) because Petersen ('541) explains it helps release the analyte from the cells for further analysis or purification (column 2, lines 1 – 3).

19. Claims 23 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swerdlow et al. (US 5,935,522) in view of Goodale et al. (US 5,356,525) as applied to claim 22 and 42 respectively, above and further in view of Petersen et al. (US 6,391,541).

Regarding claim 23, Swerdlow ('522) further discloses the liquid source further comprising: a hydraulic system adapted for control by an automated controller (130), comprising a pump (100) and one or more valves (105, 108); a rough filter selected to separate from the macromolecule in a liquid mixture comprising the macromolecule, at least a portion of one or more rough components in the mixture that are larger than the macromolecule (column 5, lines 36 – 41); a fine filter (106) selected to separate from the macromolecule in a liquid mixture comprising the macromolecule, at least a portion of one or more fine components in the mixture that are smaller than the macromolecule (column 9, lines 2 – 6); and the hydraulic system being controlled to create the liquid

sample (column 11, lines 53 – 62), the liquid sample comprising the macromolecule (column 4, lines 18 – 23), by applying the liquid mixture to each filter (column 4, lines 51 – 54), with a pressure differential across each filter (column 7, lines 6 – 8).

Swerdlow ('522) discloses the use of either a rough filter or a fine filter however Swerdlow ('522) does not explicitly disclose the use of both rough and fine filters in the apparatus.

Petersen ('541) teaches the use of both rough and fine filters (column 9, lines 14 – 20).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) in view of Goodale ('525) to include both rough and fine filters as taught by Petersen ('541) because Petersen ('541) explains the rough filter has the benefit of filtering out coarse material while the fine filter filters out molecules smaller than the target macromolecule (column 9, lines 14 – 20).

Regarding claim 43, Swerdlow ('522) further discloses the method comprising: acquiring a liquid mixture (column 6, lines 54 – 57), the mixture comprising the macromolecule (column 4, lines 18 – 23), one or more rough components that are larger than the macromolecule (column 5, lines 36 – 41), and one or more fine components that are smaller than the macromolecule (column 8, line 55 – 66); creating the liquid sample, by separating from the macromolecule at least a portion of the components by applying the mixture to each of a plurality of filters (column 8, lines 25 – 27), with a pressure differential across each filter (column 7, lines 6 – 8), the filters

comprising a rough filter selected to separate at least a portion of the rough components (column 5, lines 36 – 41) and a fine filter (106) selected to separate at least a portion of the fine components (column 9, lines 2 – 6).

20. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Swerdlow (US 5,935,522) in view of Petersen et al. (US 6,391,541), Chow et al. (US 6,537,799) and Goodale et al. (US 5,356,525).

Regarding claim 45, Swerdlow ('522) discloses an apparatus for electrophoretic separation of a macromolecule (abstract and Fig. 1), comprising: a plurality of valves (105, 108, 147, 122); a fine/desalination circuit, comprising a fine pump (100), a reservoir (102) that supplies a desalination buffer (column 16, lines 17 – 21), and a fine filter (106) selected to separate fine components from the macromolecule (column 9, lines 2 – 6); a denaturation circuit comprising a denaturation pump (100), a denaturing vessel (104) comprising a heating element and a cooling element (column 5, lines 2 – 22), a capillary electrophoresis circuit comprising an inlet chamber (112) and an outlet chamber (120), the chambers each comprising an inlet valve (108, 122), an output valve (147, 122), and an electrode (column 5, lines 46 – 66 and column 11, lines 53 – 60), the electrodes coupled to a power supply (128); a capillary electrophoresis column (116), having a length of at least about 20 centimeters (column 10, lines 43 – 48), the opposite ends of the column being fixed at the interior of the respective chambers (column 8, lines 29 – 33 and column 8, lines 39 – 43); a buffer reservoir (110, 120) supplying the chambers; an automated controller (130) in electronic communication with the pumps

(100, 111, 145, 124), the elements, the valves (105, 108, 113, 147, 122), the sensors (118) and the power supply (128) that controls the apparatus to: acquire a liquid mixture from a sampling site (103), the mixture comprising a macromolecule, rough components, and fine components (column 17, lines 55 – 65); separate at least a portion of rough components from the macromolecule in the rough separation circuit (column 5, lines 36 – 41); separate at least a portion of fine components from the macromolecule in the fine/desalination separation circuit (column 5, lines 30 – 35), the fine components comprising salt components (column 8, lines 55 – 65); denature the macromolecule in the denaturation circuit (column 4, line 64 – column 5, line 2); and electrophoretically separate the denatured macromolecule from other components by employing the capillary electrophoresis circuit (column 5, lines 46 – 66).

Swerdlow ('522) discloses the use of a rough separation circuit in the alternate with regards to a fine separation circuit (column 5, lines 30 – 41) and hence does not explicitly disclose the details of a rough separation circuit.

Petersen ('541) teaches a rough separation circuit comprising a rough pump (105, 116, 118), a first stage rough filter (94) selected to separate rough components (column 8, lines 4 – 9), and a second stage rough filter (97, 100) selected to separate rough components that pass through the first stage rough filter (column 8, lines 12 – 30).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) to include the rough separation circuit as taught by Petersen ('541) because Petersen ('541) explains the first rough filter filters out coarse

material such as salt crystals, cellular debris, hair, tissue, etc. and the second rough filter traps the target cells or viruses in the chamber for further treatment such as lysis (column 9, lines 13 – 30).

Swerdlow ('522) discloses a denaturation circuit comprising a denaturation pump (100), a denaturing vessel (104) but does not disclose a precipitation pump, a reservoir supplying a denaturation buffer, a reservoir supplying a pH buffer and a precipitation filter selected to separate insoluble denaturation precipitate components.

Petersen ('541) discloses a denaturation circuit comprising a denaturation pump (105, 116, 118), a reservoir supplying a denaturation buffer (67), a reservoir supplying a pH buffer (66) and a precipitation filter (94) selected to separate insoluble denaturation precipitate components (column 8, lines 4 – 9).

It would have been obvious to one of ordinary skill in the art to have modified the denaturation circuit in the apparatus of Swerdlow ('522) to include the components taught by Petersen ('541) because Petersen ('541) explains they help release the analyte from the cells for further analysis or purification (column 2, lines 1 – 3).

Swerdlow ('522) does not explicitly disclose a pH sensor in the denaturation circuit.

Chow ('799) teaches a pH sensor (column 29, lines 5 – 26).

It would have been obvious to one of ordinary skill in the art to have modified the denaturation circuit in the apparatus of Swerdlow ('522) to include the pH sensor of Chow ('799) because it has the benefit of determining the pH of a fluid in a micro-scale channel as explained by Chow ('799) (column 11, lines 43 – 46).

Swerdlow ('522) does not explicitly disclose a fluid level sensor at each chamber.

Goodale ('525) teaches a fluid level sensor (column 16, lines 25 – 43).

It would have been obvious to one of ordinary skill in the art to have modified the apparatus of Swerdlow ('522) to include a fluid level sensor in each chamber as taught by Goodale ('525) because Goodale ('525) explains it provides the benefit of detecting and controlling the level of liquid in the chambers (column 3, lines 56 – 60).

Conclusion

21. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Welch et al. (US 5,302,264) discloses capillary electrophoresis (CE) system with pressure regulation using pumps and valves.

Lauer et al. (US 5,217,590) discloses CE system with automatic fluid injection using pressure module.

Yeung et al. (US 6,387,234) discloses integrated chromatography and CE system with automation.

Wilding et al. (US 6,953,676) discloses all details of claimed denaturation circuit.

Zanzucchi et al. (US 5,593,838) discloses cell lysis apparatus and method.

Shand et al. (US 5,902,796) discloses method steps of the instant application.

EP 0249932 A2 discloses automated purification process.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Surekha Vathyam whose telephone number is 571-272-2682. The examiner can normally be reached on 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam X. Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SV
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